REMARKS

Applicants herein traverse and respectfully request reconsideration of the rejection of the claims in view of the following remarks.

Claims 34-42 have been rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent 5,048,727 (Vlasich) in view of U.S. Patent 3,709,365 (Czaplinski et al.) In particular, the Examiner states:

> Vlasich discloses a pharmaceutical package as seen in figure 1, which comprises a closed polypropylene bottle/barrel (12) in which is disposed a solution (15), the solution comprises a pharmaceutical product (col. 2, ll. 57-64), wherein the solution does not fill the bottle completely and some air is disposed in the bottle (col. 3, ll. 34-39). Vlasich lacks after autoclaving the package at at least 121°C and for at least 20 minutes, suffers no deformation, does not shrink, and does not explode and where the package retains a sufficiently high squeezability to dispense the solution. Czaplinski et al. teach the use of autoclaving a polypropylene material at about 115 -125°C. from 20-30 minutes (col. 2, ll. 49-58).
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> It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify Vlasich's package by autoclaving the package, as taught by Czaplinski et al. in (col. 2, ll. 49-58) in order to treat a material that can withstand autoclaving at a temperature 121°C for at least 20 minutes.

Applicants disagree with the Examiner's conclusion and respectfully submit that the combined cited references do not make obvious the claimed subject matter as defined in independent Claim 34.

Before discussing each of the cited references, the Examiner's attention is directed to MPEP §2141.02, which indicates that when ascertaining the differences between the prior art and the claims at issue, not only must the claimed invention be considered as a whole, but also the prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. To this end, the statements made by the Examiner at Pages 2-3 when discussing the Vlasich and Czaplinski et al. disclosures, clearly show that he is not considering the Vlasich or the Czaplinski et al. disclosure as a whole, but instead has chosen certain features from the cited references and has compared them to certain features of the claimed invention. Applicants respectfully submit that the presently claimed pharmaceutical package viewed as a whole is completely different from the dispenser of Vlasich viewed as a whole and is not made obvious by the combination of Vlasich and Czaplinski et al.

Vlasich describes a single dose (also called unit dose) dispenser for dispensing a predetermined product dose. The single dose dispenser is capable of discharging an entire predetermined dosage of a composition by preventing residual quantities of the composition from remaining in the dispenser. Vlasich indicates that this single dose dispenser overcomes the problem with prior art single dose dispensers wherein residual amounts of the composition remained in the dispenser following pressure that was applied to the container of the dispenser.

The single dose dispenser of Vlasich as shown in Figure 1 and described in column 2, lines 16-56 and column 3, lines 34-68 to column 4, lines 1-45, is made up of two different chambers: 1) a compressible container (12) filled with a gas propellant such as air, and 2) a product dispensing storage tube (14) filled with a predetermined dose of a composition (15) to be dispensed. The tube (14) includes a discharge opening (19) and is connected to the compressible container (12). By compressing the container (12) the air contained therein is forced to flow into the tube (14) to displace the composition (15) from the tube through the discharge opening (19). The wall (20) of the container (12) is made of a material having sufficient flexibility such as polyethylene, polypropylene, polyvinyl chloride, copolymers and the like, to permit it to bow inwardly upon application of finger pressure. The tube side wall (24) is of sufficient rigidity to resist the tendency to blow upon application of finger pressure. The composition (15) is thus prevented from being inadvertently squeezed into the container (12) filled with air. Accordingly, the single dose dispenser of Vlasich is made up of two different chambers, 1) a flexible chamber containing air, and 2) a rigid chamber containing the composition. As seen from the description of the single dose dispenser, Figure 2 and the Brief Description of the Drawings for Figure 2, once the wall (20) of the container (12) is compressed all the air in the container is displaced and the container is in a collapsed state to dispense all of the unit dose of the product contained in the tube (14). It appears apparent from Vlasich that once the container is compressed and the air flows out, the container remains in the collapsed state since all the air is pushed out into the tube and since it is likely that a residual amount of the composition could end up flowing back into the container if the container remained squeezable. Importantly, the single dose dispenser is utilized one time to dispense the entire predetermined dosage from the dispenser.

Accordingly, Vlasich is only concerned with dispensing an entire predetermined dosage in one single discharge. The single unit dosage dispenser of Vlasich does not need to retain sufficient squeezability because the dispenser is designed to be squeezed once to discharge the entire predetermined dose from the container. As acknowledged by the Examiner there is no teaching or specific suggestion in Vlasich of autoclaving the dispenser containing the composition at at least 121°C.

In contrast to the two-chamber dispenser of Vlasich wherein the air and composition are in two different chambers and the two different chambers are made of different materials, the presently claimed pharmaceutical package comprises a closed bottle, i.e., one chamber, made of polypropylene, wherein the one chamber, the bottle, contains both the solution or gel comprising a pharmaceutical product and air. Further, in contrast to the dispenser of Vlasich which is utilized once to dispense the entire composition, the pharmaceutical package as set forth in independent Claim 34 is utilized repeatedly to dispense the pharmaceutical product out of the package one drop at a time. Accordingly, the presently claimed pharmaceutical package upon autoclaving must retain sufficient squeezability to deliver repeatedly the pharmaceutical product. That the pharmaceutical package must retain sufficient squeezability for its repeated use is clearly set forth in the specification at Page 2, the second full paragraph from the bottom of the page, wherein it states:

> Packages made of a specific form of polypropylene are heat-resistant and retain their formation and their squeezing characteristics after the autoclaving processing. Therefore, the consumer can easily dispense <u>one drop at a time</u> [emphasis added] by squeezing the package so as to force the pharmaceutical product out of the package.

Accordingly, the two-chamber dispenser of Vlasich which is utilized one time to dispense an entire predetermined dosage is completely different from the closed, one-chamber polypropylene bottle of Claim 34 which is utilized repeatedly, i.e., one drop at a time. In view of the differences between the dispenser of Vlasich and the pharmaceutical package of Claim 34 one skilled in the art reading Vlasich as a whole would not equate the dispenser with the presently claimed pharmaceutical package.

Applicants also respectfully direct the Examiner's attention to the Federal Court's instruction in *In re Gurley*, 31 USPQ2d 1131 (Fed. Cir. 1994), wherein the Court instructed that a prior art reference "teaches away" when one of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the prior art reference, or alternatively, would be led in a direction divergent from the path that was taken by the applicant.

In view of the above instruction, it can fairly be said that Vlasich, in teaching use of a single unit dose dispenser in which the container portion of the dispenser collapses upon exerting pressure on the container, specifically teaches away from the presently claimed pharmaceutical package which must retain sufficient squeezability for repeated use so that it can easily dispense the pharmaceutical product out of the package one drop at a time. Accordingly, one skilled in the art armed with the teaching of Vlasich would be led in a direction divergent from the path that was taken by the Applicants, that is, one skilled in the art would not

have chosen to construct a pharmaceutical package that retains sufficient squeezability to repeatedly dispense the pharmaceutical product one drop at a time.

Accordingly, in view of the vast differences between the dispenser of Vlasich and the claimed pharmaceutical package, and the teaching away in Vlasich from utilizing a polypropylene bottle that retains sufficient squeezability to repeatedly dispense the pharmaceutical product one drop at a time, one skilled in the art reading the Vlasich disclosure as a whole would not be motivated to utilize Vlasich to arrive at the presently claimed pharmaceutical package.

Czaplinski et al. describe a radioactive generator system having a sterile, sealed disposable closure therein. As shown and described in Figure 1 and column 2, lines 3-62 of Czaplinski et al., the generator system (4) is connected to an elution bottle (12) containing an elution solution (10) via a hypodermic needle. The details of the generator system (4) are more fully set out in U.S. Patent 3,369,121 (Bruno et al., a copy of which is attached) which is referenced in Czaplinski et al. (see column 2, lines 9-11). As described in Bruno et al., the generator system houses a column which has bound to it radioactive material (see columns 2 and 3). As further described in Bruno et al. (see column 3, lines 62-75), the column, prior to its insertion in the generator system, is filled with a radioactive solution. Most of the radioactive material is absorbed onto the column and the excess radioactive material and water pass through the column and are removed. The column is then washed with acid and saline to remove any non-absorbed radioactivity and the column is sterilized, as by autoclaving. Following autoclaving, the sterilized column containing the bound radioactive material is inserted into the body of the generator.

As further described in Czaplinski et al. (see column 2, lines 3-62), the eluting solution contained in the elution bottle which is hooked up to the generator system flows through the sterilized column of the generator system and the eluate containing the radioactive material is removed via a hypodermic needle from the bottom of the generator system and allowed to pass through conduit (22) into sterile closure (30) and then through conduit (24) into vial (20).

The sterile closure (30) comprises *inter alia*, a housing (42) wherein one end is closed by a pierceable membrane and the opposite end remains open, a membrane filter placed between the membrane and the open end, and a seal around the closed end of the housing (42) to retain the membrane in position. The purpose of the sterile closure (30) is to ensure sterility at the site of delivery of the radioactive material and reduce contamination of the generator system (see Czaplinski et al., column 1, lines 41-50).

Czaplinski et al. (see column 2, lines 49-55) indicate that the housing material (42) can be made of a plastic, e.g., polypropylene or metal material which withstands autoclaving, e.g., about 115-125°C. As is apparent from Czaplinski et al., the sterile closure (30) comprising *inter alia* the housing material (42) made of plastic or metal is sterilized prior to being connected to conduits (22) and (24). Further, the radioactive material eluting from the column has already been sterilized prior to its elution from the column and is not sterilized at 115-125°C when it passes through the housing material (42) of the sterile closure (30). Thus, the radioactive material eluted from the column is not contained in the closure (30) when the closure (30) is sterilized. Accordingly, Czaplinski et al. is not concerned with the problem of autoclaving a closed polypropylene package which has disposed therein a solution or gel comprising a pharmaceutical product. As stated above, Czaplinski et al. is merely concerned with the problem of ensuring sterility at the site of delivery of the radioactive material and to reduce contamination of the generator system. Accordingly, Czaplinski et al., as a whole, does not describe the sterilization of a closed polypropylene bottle containing material therein as is recited in the presently claimed invention. Further, there is absolutely no requirement that the housing material (42) of Czaplinski et al. retain sufficient squeezability.

Accordingly, it is difficult to see how one skilled in the art reading the Vlasich and Czaplinski et al. as a whole, would be motivated to combine these references and arrive at the pharmaceutical package defined in Claim 34.

Further, it is submitted that the Examiner, 1) in arguing that Vlasich describes a closed polypropylene bottle containing a pharmaceutical product and air, rather than considering that Vlasich as a whole actually describes a two-chamber, unit dose dispenser, and 2) in selecting from the complete generator system described in Czaplinski et al. a polypropylene housing material (42) which can withstand autoclaving at 115-125°C, appears to be selecting particular features of the cited references to piece together the invention. In this regard, Applicants respectfully direct the Examiner's attention to the Federal Court's instruction in *In re Fine*, 847 F. 2d, 1071, 5USPQ2d 1596 (Fed. Cir. 1988) wherein the Court instructed that "One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention."

Accordingly, Vlasich and Czaplinski et al., each taken alone or combined, do not make obvious the pharmaceutical package defined in Claim 34.

In view of the above, withdrawal of the rejection of Claims 34-42 under 35 U.S.C. §103(a) is respectfully requested.

A good faith effort has been made to place the present application in condition for allowance. If the Examiner believes a telephone conference would be of value, he is requested to call the undersigned at the number listed below.

Respectfully submitted,

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